

Notice of Allowability

Application No.

09/869,696

Examiner

Maria B. Marvich, PhD

Applicant(s)

DAVIES, DONALD

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 12/22/05.
2. ☒ The allowed claim(s) is/are 41-54,56,57,59-61,63,65-76,78,79,81 and 84-87.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
- ☒ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

Art Unit: 1633

Allowance

This office action is in response to an after-final amendment filed 12/22/05. The amendment has been entered. Claims 1-40, 55, 58, 62, 64, 77, 80, 82 and 83 have been canceled. Claims 41, 60 and 85 have been amended. Claims 41-54, 56, 57, 59-61, 63, 65-76, 78, 79, 81 and 84-87 are pending.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Kenning Li on January 20, 2006.

The application has been amended as follows:

IN THE CLAIMS:

In claim 41, line 8, the phrase "exhibits an activity of converting" prior to "acetaminophen to a cytotoxic molecule" has been deleted and replaced with the phrase --is expressed in an effective amount to convert--.

In claim 42, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

Art Unit: 1633

In claim 43, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

In claim 44, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

In claim 45, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

In claim 46, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

In claim 46, line 3, the words "lenti virus" prior to the phrase "and baculovirus" has been deleted and replaced with the word --lentivirus--.

In claim 47, line 1, the word "A" prior to the phrase "method according to" has been deleted and replaced with the word --The--.

In claim 47, line 11, the phrase "tumor rejection antigen precursor promoters" following the phrase "tyrosine related peptide promoter, and" has been deleted and replaced with the phrase -- tumor rejection antigen precursor promoter--.

Art Unit: 1633

In claim 48, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 49, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 50, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 50, line 4, the phrase “tumor rejection antigen precursor promoters” following the phrase “tyrosine related peptide promoter, and” has been deleted and replaced with the phrase -- tumor rejection antigen precursor promoter--.

In claim 51, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 52, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 53, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 53, line 2, the phrase “of mammalian origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a mammalian polynucleotide --.

In claim 54, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 54, line 2, the phrase “of human origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a human polynucleotide--.

In claim 56, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 57, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 57, line 2, the phrase “of rodent origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a rodent polynucleotide--.

In claim 59, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

Art Unit: 1633

In claim 59, line 2, the word “cancers” following the phrase “and retinal” has been deleted and replaced with the phrase -- cancer--.

In claim 60, line 9, the phrase “exhibits an activity of converting” prior to “acetaminophen to a cytotoxic molecule” has been deleted and replaced with the phrase --is expressed in an effective amount to convert--.

In claim 63, line 3, the phrase “having an activity of converting acetaminophen to a cytotoxic molecule,” following the phrase “CYP1A2, CYP2E1, CYP3A4” has been deleted and replaced with the phrase -- , wherein the polypeptide converts acetaminophen to a cytotoxic molecule, and--.

In claim 65, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 66, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 67, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

Art Unit: 1633

In claim 68, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 69, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 69, line 8, the phrase “tumor rejection antigen precursor promoters” following the phrase “tyrosine related peptide promoter, and” has been deleted and replaced with the phrase -- tumor rejection antigen precursor promoter--.

In claim 70, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 71, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 72, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 72, line 5, the phrase “tumor rejection antigen precursor promoters” following the phrase “tyrosine related peptide promoter, and” has been deleted and replaced with the phrase -- tumor rejection antigen precursor promoter--.

Art Unit: 1633

In claim 73, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 74, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 75, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 75, line 2, the phrase “of mammalian origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a mammalian polynucleotide--.

In claim 76, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 76, line 2, the phrase “of human origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a human polynucleotide--.

In claim 78, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

Art Unit: 1633

In claim 79, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 79, line 2, the phrase “of rodent origin” following the phrase “said polynucleotide is” has been deleted and replaced with the phrase -- a rodent polynucleotide--.

In claim 81, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 84, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 85, line 8, the phrase “exhibits an activity of converting” prior to “acetaminophen to a cytotoxic molecule” has been deleted and replaced with the phrase --is expressed in an effective amount to convert--.

In claim 86, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

In claim 87, line 1, the word “A” prior to the phrase “method according to” has been deleted and replaced with the word --The--.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: the present invention advances the prior art by design of a method for inhibiting the growth of cancerous cells or for selectively killing cells in a mammal by combination therapy using introduced P450 such as CYP1A2, CYP2E1 or CYP3A4 in combination with exogenous acetaminophen. Acetaminophen is converted to N-acetylbenzoquinoneimine (NABQI), which is a cytotoxic molecule by P450 resulting in cell death. The method of the invention is most similar to the invention of Rubin, US 5,760,008. The difference between the two is that the instant invention is drawn to gene therapy for introduction of exogenous P450 combined with administration of sufficient levels of acetaminophen to produce cytotoxic levels of NABQI while Rubin et al teaches a different direction for cell killing. Rubin et al engineers conjugated substrates for P450 that render the substrates non-toxic till presented to the cancer cell where it is hypothesized P450 metabolizes them to produce toxic by products. The effectiveness of this method is not demonstrated. In a declaration filed 1/24/05, applicants have demonstrated that mCYP1A2/acetaminophen is an effective cytotoxic mechanism *in vivo* but no cell killing was evidenced in the absence of exogenous P450. As set forth in the office action mailed 2/24/05 there is a general recognition that gene therapy per se is not routine and must be evaluated on a case-by-case basis. Furthermore, the art does not teach or suggest combination therapy comprising administration of exogenous P450 and acetaminophen and absent a demonstration that exogenous P450 is required to elevate levels of NABQI, there would be no motivation to require administration of P450 for effective cytotoxicity. Therefore, the instant invention is drawn to a method for the production

Art Unit: 1633

of sufficient levels of NABQI for cytotoxicity by the combination of CYP1A2, CYP2E1 or CYP3A4 and acetaminophen.

Art Unit: 1633

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 41-54, 56, 57, 59-61, 63, 65-76, 78, 79, 81 and 84-87 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

January 19, 2006


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